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RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

Second Annual National Conference

September 30 – October 2, 2021

Phoenix, AZ

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Complex Management of Myositis

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Faculty Disclosure

- Michele Cerra, MSN, FNP-BC:
  - Consultant: Abbvie, Janssen, Eli Lilly, AstraZeneca, Amgen, Novartis, Sanofi Genzyme
- Erin Siceloff, PA-C:
  - Speaker: Abbvie, Novartis
  - Consultant: Pfizer

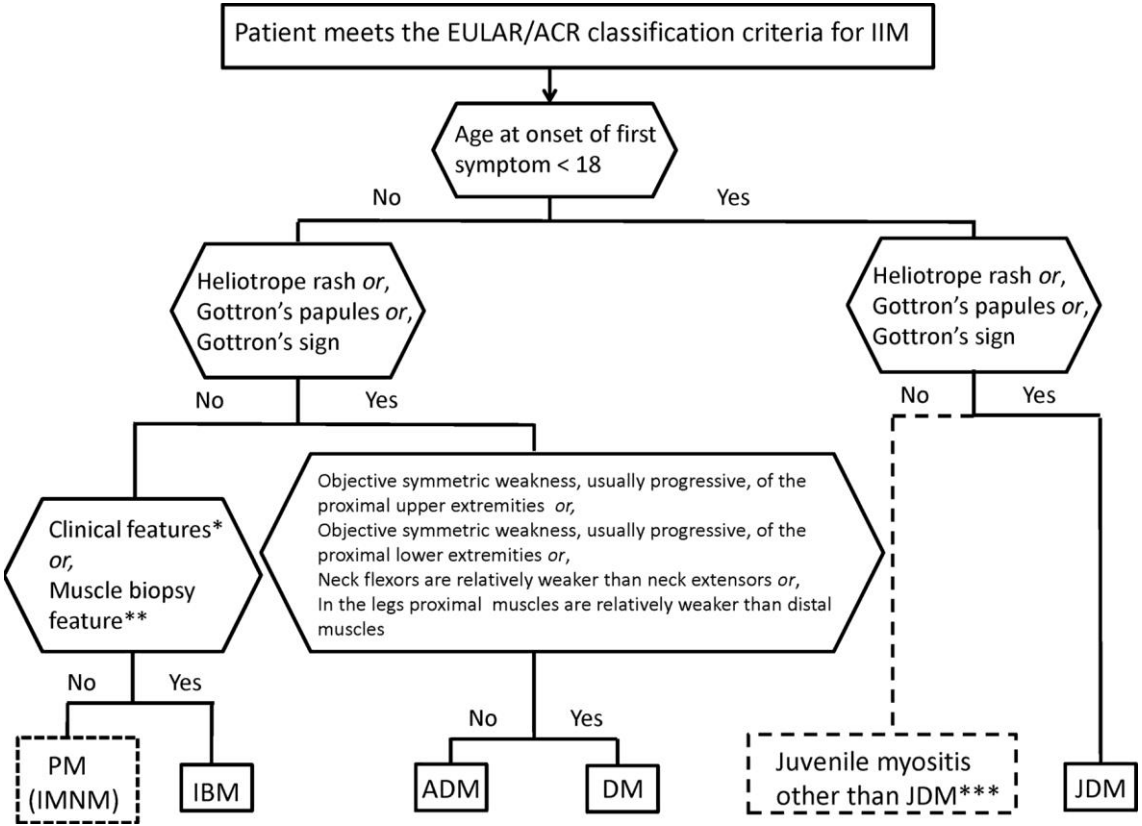
Inflammatory Myopathies

- Inflammatory myopathies are characterized by muscle weakness specifically due to muscle inflammation
- Classifications of inflammatory myopathies include:
  - Polymyositis
  - Dermatomyositis
  - Amyopathic Dermatomyositis
  - Inclusion Body Myositis
  - Juvenile Myositis

PM/DM: Diagnostic Criteria
Bohan and Peter (1975)

Criteria	Description
A	Proximal and symmetrical muscle weakness of the pelvic and scapular girdle, anterior flexors of the neck, progressing for weeks to months, with or without dysphagia or involvement of respiratory muscles
B	Elevation of the serum levels of skeletal muscle enzymes: creatine kinase, aspartate aminotransferase, lactate dehydrogenase and aldolase
C	Electromyography characteristic of myopathy (short and small motor units, fibrillation, positive pointy waves, insertional irritability and repetitive high-frequency firing)
D	Muscle biopsy showing necrosis, phagocytosis, regeneration, perifascicular atrophy, perivascular inflammatory exudate
E	Typical cutaneous changes: (1) Heliotrope rash with periorbital oedema and violaceous erythema (2) Gottron's sign: vasculitis in the elbow, metacarpophalangeal and proximal interphalangeal joints
Polymyositis	(1) Definite – all of A-D (2) Probable – any three of A-D (3) Possible – any two of A-D
Dermatomyositis	(1) Definite – E plus and three of A-D (2) Probable – E plus and two of A-D (3) Possible – E plus and one of A-D

EULAR/ACR Updated Classification Criteria – 2017



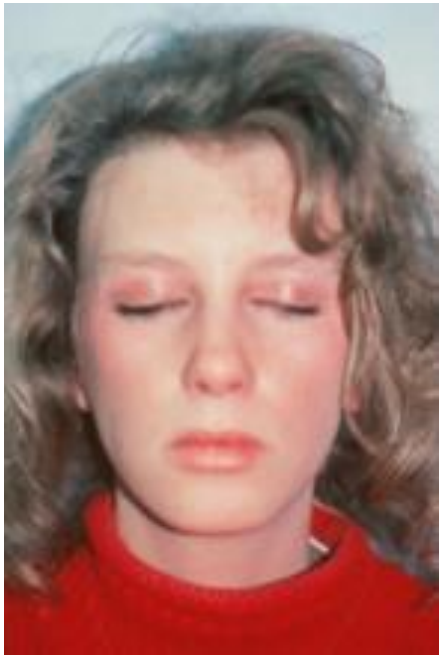
EULAR/ACR Updated Classification Criteria – 2017

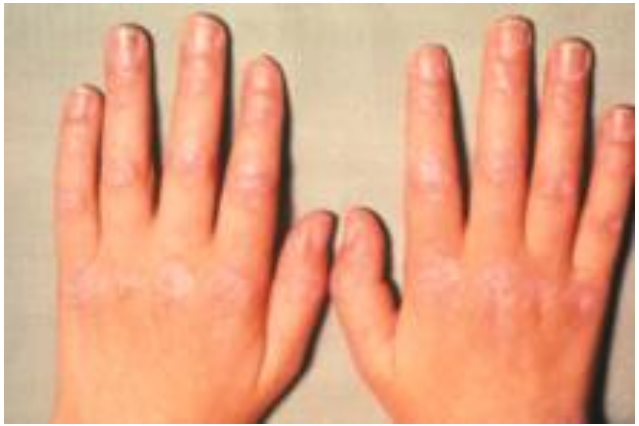
- www.imm.ki.se/biostatistics/calculators/iim

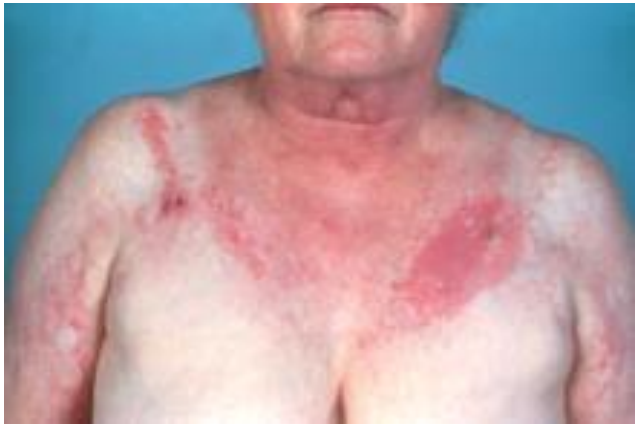
Diagnosis

- Clinical symptoms including muscle weakness of proximal muscles
- Lab values including marked elevated of CK, and sometimes other enzymes such as LDH, AST or ALT; other myositis specific autoantibodies may be detected
- EMG of affected muscles displays a myopathic pattern
- MRI can be helpful to identify areas of active muscle inflammation. This can help determine the appropriate muscle site to biopsy
- Muscle biopsy – This is the most important and most invasive step to make the correct diagnosis and is the only way to distinguish between the different subtypes of myositis (which is important when considering treatment options).

Typical DM Rashes

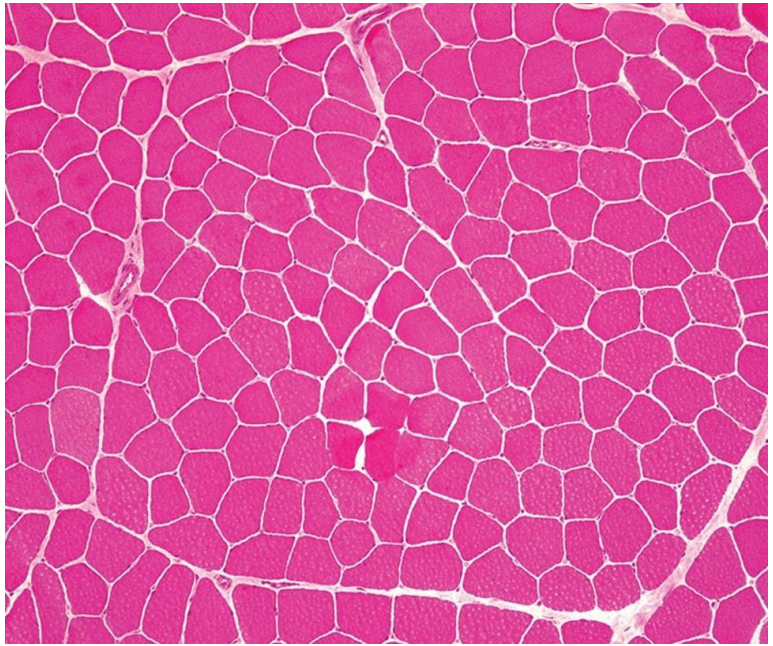


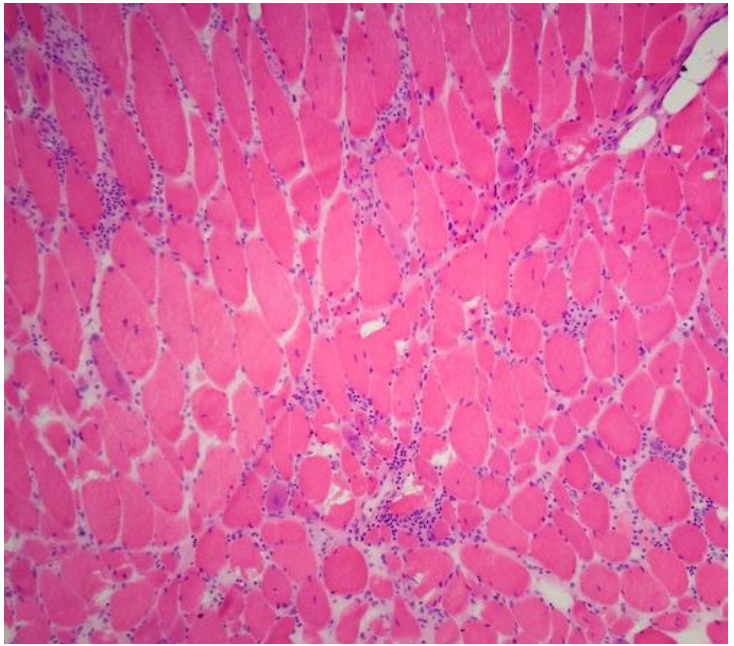




ACR Image Library. Available at: https://www.rheumatology.org/Learning-Center/Rheumatology-Image-Library. Accessed November 2, 2020.

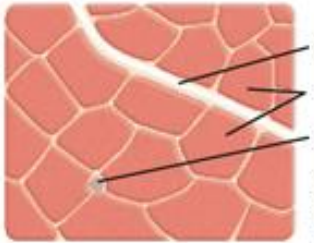
Pathology





Pathology

Normal Muscle



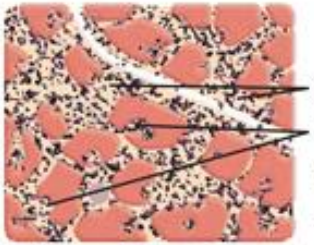
border of muscle bundle (fascicle)

normal muscle fibers

blood vessel

When normal muscle fibers are viewed under a microscope, they look like puzzle pieces that fit together neatly.

Polymyositis



inflammatory cells

invasion of fibers by inflammatory cells

In polymyositis, inflammatory cells of the immune system invade previously healthy muscle cells, which become rounded and varible in size.

Epidemiology

- Incidence of PM and DM 2 per 100,000 annually in the generally population
- Prevalence of PM and DM 5-22 per 100,000
- Female: Male = 2:1 for PM/DM
- Peak Incidence of PM and DM in adults occurs between 40-50 yo, but individuals of any age may be affected
- DM has bimodal distribution with peak of onset in < 18 yo and again in midlife

Clinical Manifestations

MSK	Cutaneous	Extramuscular
Symmetric Proximal Muscle weakness	Photosensitive Rashes	Fever/chills, fatigue, and weight loss
Dyspnea due to diaphragmatic and intercostal muscle weakness	Heliotrope Rash; Shawl Neck sign	Raynaud's phenomenon
Dysphagia due to pharyngeal muscle weakness	Grottron's papules; Mechanics hands	Inflammatory arthritis
	Cuticle Hypertrophy	ILD
	Nailfold Capillary Abnormalities	GI and Cardiac Manifestations

Treatment

- Glucocorticoids – 1st line of treatment for PM/DM
  - Reduce muscle inflammation thus improving muscle symptoms including weakness
  - 1 mg/kg until stable ~ 4-12 weeks or longer.
  - Reduction by 10 mg every 1-2 weeks until~ 20 mg
  - From 20 mg/day, taper is slowed to 2.5-5 mg/day every 1-2 weeks.
- Maintenance dose of 5 mg/day often necessary.
- Initial IV pulse therapy at 0.5-1 g/day for 3-5 days.

Treatment

Immunosuppression therapy combined with GCs:

1. Methotrexate (MTX): 20-25mg po/sc once weekly
2. Azathioprine (AZA): 50 mg/day with incremental increase by 25-50 mg every 1-2 weeks up to 2 mg/kg daily.
3. Mycophenolate mofetil (MMF): 500 mg bid up to 2-3 g daily dose refracted in two daily doses.

Additional/Alternate Therapy

1. Intravenous Immunoglobulins (IVIG)
   - MOA Unknown
   - 1 g/kg every 4-8 weeks (1-2 g/kg)
   - Expense of this treatment is an important consideration in its long-term use
   - May be combined with other immunosuppressive drugs
   - Generally well tolerated and considered relatively safe

Additional/Alternate Therapy

2. Calcineurin Inhibitors: Main effects are the inhibition of T cell activation and T cells play an important role in the pathogenesis of PM/DM
   - Cyclosporine-A (CYA) – Administered po 2-4 mg/kg/day divided in 2 daily doses
   - Tacrolimus (TAC) 1 mg bid until target blood levels of 5-20 ng/ml are reached

Therapy Escalation

1. Rituximab: Targets CD20 +cells, B-cell precursors
   - Less costly than IVIG
   - Has been associated with substantial improvement
   - Most commonly used biologic in the treatment of PM
   - Dosed as two 1000mg infusions 2 weeks apart (May be repeated after 6 months)
2. Cyclophosphamide: 500 mg IV qow up to 12 doses

Treatment

OTHER THERAPIES:

1. HCQ: Up to 400 mg QD
2. IV Abatacept
3. IL-6 Inhibitor (Tocilizumab)
4. TNF inhibitors ??

Treatment

- Non-Pharmacological Treatment
  - Exercise
  - Physical Therapy – Should be initiated as soon as possible after the start of immuno-suppressive treatment.

Questions

Thank You!

References

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